

Attorney Docket No. P69482US1  
Application No. 10/581,547

Remarks/Arguments:

Applicants wish to thank the examiner for effecting the renumbering of originally filed claims 25-29 to become claims 24-28 presented by preliminary amendment filed April 14, 2008.

Claims 1-3, 5-7, 18, and 20-24 are pending, with claims 18 and 20-24 being withdrawn (but rejoinalable) pursuant to restriction.

Claims 4, 8-17, 19, and 25-28 are cancelled, with claims 8-14 being cancelled pursuant to restriction.

By the instant amendment the specification and claims are amended, as set forth above. Specifically, the term "Seq. Id. No." has been substituted by "SEQ ID NO:" in the specification as well as in the claims and, in the claims, the term "anti-progesterons" has been substituted by the term "anti-progesterones," the RNA has been specified "mRNA," the term "alcaloid" has been substituted by the term "alkaloid", the term "estrogenes" replaced by the term "estrogens", the term "anti-progesterons" has been substituted by the term "anti-progesterones", and the term "mifepriston" by the term "mifepristone". The claims are also amended to correct other non-English spellings appearing in the claims and to, otherwise, more clearly define the instant invention.

The specification and claims are objected to for reciting "Seq. Id. No." instead of "SEQ ID NO:". Claims 1 and 7 were also objected to for containing non-English spellings of certain biochemical terms (listed at page 4 of the instant Office Action). In view of the changes to the instant specification and claims, as explained above, the objections thereto are overcome. Withdrawal of the objections appears to be in order.

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Claim 4 was rejected under 35 USC § 112, 2<sup>nd</sup> paragraph, as allegedly being indefinite for limiting the recited "oligonucleotide" to one or more sequences corresponding to numbers "1-147" found in the Sequencing Listing. Claims 1-3, 5, and 6 were rejected under 35 USC § 103(a) as being allegedly unpatentable over Roth et al. (Cellular and Molecular Life Sciences, 56, 1999, 481-506). Claims 1-3, 5, and 6 were also rejected under 35 USC § 103(a) as being allegedly unpatentable over Roth et al. in view of Jachimczak et al. (Int. J. Cancer, 65, 1996, 332-337). Reconsideration of the rejections is requested.

Applicants submit that the rejection under §112, ¶2, and both rejections under §103(a) are overcome in view of amending the claims, hereby, to recite "the oligonucleotide comprises at least one of the sequences of SEQ ID NO: 1-78." That is, the present claims (as amended) literally limit the "oligonucleotide"—alternatively recited as "TGF-beta agonist" component of the claimed composition—"hybridising" with TGF- $\beta$  nucleic acid sequences, which satisfies the requirements of §112, ¶2, and §103(a) with respect to the presently claimed invention.

As to the §103(a) based on Roth et al., alone, the reference describes the combination of chemotherapy and immunotherapy as a potential alternative either (1) to combinations of chemotherapies including two or more cytotoxic drugs or (2) to an immunotherapy. However, according to Roth et al. none of the polychemotherapies have been shown to be superior to BCNU monotherapy or PCV polychemotherapy (Roth et al., p. 483, left col., end of 2<sup>nd</sup> paragraph) and, further, all clinical trials based on immunotherapy have been disappointing in the treatment of malignant glioma (Roth et al., p. 483, right col., end of 3<sup>rd</sup> paragraph).

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For the combination of chemotherapy and immunotherapy in an immunochemotherapy, Roth et al. suggest that most of the combined immunochemotherapies have not led to a more efficient treatment of malignant glioma; moreover, the reference teaches that, to date, most of the combined immunochemotherapies appear not to be superior to conventional chemotherapy" (Roth et al., p. 490, left col., 2<sup>nd</sup> paragraph). Consequently, Roth et al. provide no data for immunochemotherapy comprising antisense TGF-beta, which is successful in the treatment of malignant glioma.

Hence, Roth et al. teaches away from the presently claimed invention due to the negative perspective drawn for immunochemotherapies by the reference, such that a skilled person would not continue combining chemo- and immunotherapies, in particular not with immunotherapies described in Roth et al. such as TGF-beta antisense. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). The skilled person would rather search for alternative therapies or at least for immunotherapies "in a direction divergent from" the immunotherapies disclosed in Roth et al., rendering the presently claimed invention patentable over the cited reference under §103(a). *Gurley*, 31 USPQ2d at 1131.

As to the §103(a) rejection based on Roth et al. in view of Jachimczak et al., the acknowledged failure of Roth et al. to support (i.e., specify) the *hybridising oligonucleotides* recited in the claims—as "TGF-beta antagonist" component of the presently claimed composition—is allegedly supported by Jachimczak et al., which is cited by Roth et al. (page 504).

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Given that Jachimczak et al. is cited by Roth et al. in the context of TGF-beta, the skilled person would have inferred that the antisense TGF-beta described by Jachimczak et al. had already been tested in immunochemotherapies without success. Therefore, the person skilled in the art would not at all have expected the results obtained in accordance with the presently claimed invention, such as shown in Figures 1, 2, and 4-10 of the present application, for combinations of SEQ ID NO: 30 with each of CCNU, BCNU, gemzar, temozolomide, vincristine, taxotere, and procarbazine. In other words, the skilled person would have been "discouraged from following the path set out in the [Roth et al.] reference" to work with the TGF-beta antisense disclosed in Jachimczak et al. and "would be led in a direction divergent from the path that was taken by the applicant," *Gurley*, 31 USPQ2d at 1131, which renders the presently claimed invention patentable over the combined teachings of the cited references. In fact, the skilled would have been led away from even performing research using the Jachimczak et al. TGF-beta antisense, given the negative teachings in this respect set forth in Roth et al.

Consequently, neither Roth et al., alone, nor Roth et al. combined with Jachimczak et al. would have taught or suggested the presently claimed invention. References taken in combination teach away when the combination would produce a "seemingly inoperative" result. *In re Sponnoble*, 160 USPQ 237, 244 (CCPA 1969). A "reference teaches away if it leaves the impression that the product would not have the property sought by the applicant." *Gurley*, 31 USPQ2d at 1132, citing with approval *In re Caldwell*, 138 USPQ 243, 245 (CCPA 1963). The totality of each reference's teachings must be considered when combining those teachings with the rest of the prior art. *W. L.*

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*Gore & Assoc., Inc. v. Garlock, Inc.*, 220 USPQ 303, 311 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

It is impermissible within the framework of §103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciate of what such reference fairly suggests to one of ordinary skill in the art.

*In re Hedges*, 228 USPQ 685, 687 (Fed. Cir. 1986).

With respect to the §112, ¶2, rejection, the subject matter of the present claims (as amended) is not contraindicated by the disclosure found in the instant specification as alleged in the statement of rejection.

For the foregoing reasons the rejection under §112, ¶2, and both rejections under §103(a) are overcome. Withdrawal of the rejections appears to be in order.

***Request for Examiner's Initialed Form PTO 1449***

On October 26, 2006, an Information Disclosure Statement (IDS), including completed form PTO 1449, corresponding international search report (ISR), and copies of the cited references, was filed in the PTO. The submitted PTO form 1449 signed by the examiner was attached to the instant Office Action, but with a line was drawn through each of the cited references along with the examiner's added notation "All references considered except where lined through."

Accordingly, the Examiner is requested to mark and initial the submitted Form PTO 1449 to show that the reference at issue was considered and return the initialed Form so marked to applicants' undersigned representatives.

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Favorable action is requested.

Respectfully submitted,

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